REMARKS/ARGUMENTS

Claims 1, 8, 13, 17, 21 and 25-29 are pending in the captioned application. Applicants have amended claims 1, 17 and 21 and cancelled claims 30, 36 and 37. Applicants have also added new claims 45-52. Applicants respectfully request reconsideration and allowance of the claims in view of the amendments and the following arguments.

Claims 1, 17 and 21 have been amended. Claim 1 has been amended to recite that the polymer hydrogel is negatively charged. Support can be found in the specification, see, e.g., paragraph 73 of the published US patent application, where the hydrogel is said to have an anionic character. The claim is also modified to state that the polymer hydrogel is modified with one member of a specific binding pair. See, e.g., paragraph 59. Claim 17 is amended to further clarify the claim. Claim 21 is amended to define the polymer hydrogel, see, e.g., paragraph 73.

Applicants have also added new claims 45-52. The new independent claim 45 is similar to claim 1. The difference lies in the contacting step, which is changed to: "*contacting the complex formed with the solid support surface which comprises a negatively charged polymer hydrogel containing functional groups capable of being activated, to thereby couple a oligonucleotide via reactive groups, which are part of or chemically introduced into the oligonucleotide, via a specific reaction with the activated functional groups*". Applicants submit that this is fairly supported by the

specification, see, e.g., paragraph 58. The new dependent claims do not introduce new matter either.

The claims are again rejected under 35 U.S.C. §103(a) as being unpatentable over the combined teachings of Cooper et al., Niemeyer et al., and Nikiforov et al. Applicants respectively disagree.

The Examiner argues that the disclosure of Nikiforov et al. "is not limited to hydrophobic interaction binding as the reference clearly teaches that the mechanisms are unknown …..". However, Applicants submit that Nikiforov consistently teaches means to obtain conditions for optimal hydrophobic interaction, illustrated by the following exemplary citations:

> **Col. 7, lines 35-39 and following:** *In the presence of NaCl and other salts, the hydrophobic interactions between the oligonucleotide molecule and hydrophobic regions of the polystyrene surface are enhanced to a degree that allows the immobilization of the former.*
> **Col. 7, lines 52-59:** *This association of oligonucleotides with detergents containing a hydrophobic tail will render the oligonucleotide significantly hydrophobic and will lead to immobilization to the plate surface by hydrophobic interactions. In effect these molecules appear to act as a linker between the hydrophobic areas of the plate and the charged phosphate backbone of the oligonucleotide.*
> **Col. 7, lines 63-67: …..***and since the micelles have a hydrophobic core that is completely surrounded by a polar surface, no hydrophobic interactions with the surface will occur and therefore oligonucleotide immobilization will be diminished or prevented.*
> **Col. 8. lines 10-13:** *a concentration (of salt) of at least 50 mM is desirable in order to achieve optimal immobilization (hydrophobic interactions are stronger at higher salt concentrations).*
> **Col. 12 (Example 1) lines 32-38:** *The inefficiency of NaCl in the immobilization of biotin-$(C_3)_{25}$ could be explained by the intrinsically lower hydrophobicity of this molecule compared to a typical oligonucleotide. This reduced hydrophobicity is due to the lack of deoxyribose residues and the heterocyclic bases. Thus, the presence of NaCl is not sufficient to promote hydrophobic binding of this molecule to the plate surface. On the other hand, biotin-$(C_3)_{25}$ does form complexes in solution with EDC and CTAB by*

> *electrostatic interactions. These complexes significantly increase the hydrophobicity of this polyphosphate and promote its immobilization to the polystyrene.*
> **Col. 13 (Example 2) lines 19-23:** *CTAB, on the other hand, exhibited typical cationic detergent behaviour (maximum binding at low concentration), due to its ability to act as a bridge molecule between the hydrophobic plastic and the charged phosphates of the oligonucleotide.*

Admittedly, Nikiforov teaches that the mechanisms for binding to polystyrene or glass are unknown, but as evident from the citations above he gives no guidance that e.g. a micellar complex with the oligonucleotide would work in combination with a hydrophilic hydrogel surface.

Further, in contrast to Applicants' claimed invention, Nikiforov et al. teaches means for non-covalently immobilizing oligonucleotides to polystyrene or glass solid supports. See for example: Col 8, lines 60-63: "*The immobilization mediated by these reagents is not believed to reflect covalent binding between the nucleic acid, and reactive groups of the support.*"And also Example 6. Evidence Against Covalent Binding In the Presence Of EDC.

The Examiner argues that Nikiforov teaches biotinylated oligonucleotide immobilization which in view of Cooper et al. and Niemeyer et al., who also teach immobilization of biotinylated oligonucleotides in salt solutions, it would be reasonable to use cationic detergents. However, Applicants respectfully disagree that this is obvious for the following reasons:

- Nikiforov shows examples of immobilization of biotinylated oligonucleotides. However, in contrast to Cooper and Niemeyer, Nikiforov does not teach the use of a specific binding partner like avidin or streptavidin on the surface to

mediate a specific binding (see, for example, Example 1 where a polystyrene surface was used), rather the biotin group was included to be used in later step of the assay or just as an example of a different type of oligonucleotide. Thus, the Examiner incorrectly states that they used "the same surface" and "immobilization is by binding between binding pair members".

- Also, as evident by the examples above, Nikiforov et al. teaches different means to optimize non-covalent binding without any involvement of specific binding pair but is instead utilizing hydrophobic interactions and where micelle formation should be avoided. This is in sharp contrast to the claimed invention where additions of high salt concentrations do not work but rather cationic detergents at concentrations where micelle or vesicles are formed surprisingly was the only efficient way to achieve reasonable immobilization levels.

Therefore, since Nikiforov teaches away from the use of micelle forming concentrations, the combination of Nikiforov with Cooper and Niemeyer who use standard salt containing solution would not lead to the novel findings in the claimed invention.

Applicants respectfully assert that the claims are in allowable form and earnestly solicit the allowance of the claims 1, 8, 13, 17, 21 and 25-29.

Early and favorable consideration is respectfully requested.

Respectfully submitted,

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